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Voriconazole in Dermatophytic Infections: An In-depth Examination of Its Role in Tinea Treatment

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ABSTRACT

Objective: To evaluate the efficacy of voriconazole in treating dermatophytosis, specifically tinea corporis and tinea cruris, in patients resistant to conventional antifungal treatments. The primary objective was to assess the clinical and mycological cure rates, safety, and potential impact of comorbidities on treatment outcomes.

Methodology: A retrospective analysis was conducted at Khyber Teaching Hospital, Peshawar, from June 2021 to June 2022, involving 150 patients with dermatophytosis who had failed previous treatments. Data were collected from medical records, and patients were treated with voriconazole 200 mg twice daily for a duration of 12 weeks. Follow-up visits were conducted at 2, 4, and 12 weeks.

Results: The clinical cure rate was 70%, with 50% of patients achieving mycological cure. Male patients showed a higher rate of complete resolution (45%) compared to females (40%), with a p-value of 0.003. Comorbidities such as diabetes and hypertension significantly impacted treatment outcomes, with patients without comorbidities achieving 50% complete resolution, compared to 30% and 35% in diabetic and hypertensive patients, respectively, with a p-value of 0.042. Adverse effects were reported in 25% of patients, including visual disturbances (10%), headaches (8%), and skin rashes (7%).

Conclusion: Voriconazole is an effective treatment for dermatophytosis, especially in patients resistant to conventional antifungals. The study highlights the influence of gender and comorbidity status on treatment outcomes and suggests further research to optimize treatment regimens.

Keywords: Antifungal Resistance; Dermatophytosis; Tinea Corporis; Treatment Outcomes; Voriconazole.

Authors' Contribution:
[1,2]Conception; Literature research; manuscript design and drafting; [1,2]Critical analysis and manuscript review; [1,2]Data analysis; Manuscript Editing.

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Introduction

Dermatophytosis, commonly known as fungal infections of the skin, is a prevalent dermatological condition that affects millions worldwide. Among the different species responsible for these infections, dermatophytes such as Trichophyton rubrum, Trichophyton mentagrophytes, and Microsporum canis are frequently implicated.[1,2] These fungal organisms are characterized by their ability to invade keratinized tissues like skin, hair, and nails, leading to conditions such as tinea corporis, tinea cruris, and tinea capitis. Over the years, the treatment of dermatophytosis has been increasingly challenged by the emergence of antifungal resistance, particularly against first-line treatments such as terbinafine and itraconazole. In response to this growing concern, newer antifungal agents, including voriconazole, have been explored

as potential therapies.[3,4] Voriconazole is a second-generation triazole antifungal that is widely used for treating invasive fungal infections, particularly in immunocompromised patients. However, its potential role in dermatophyte infections, particularly those caused by resistant strains, has recently garnered attention.[5,6] This novel agent works by inhibiting the synthesis of ergosterol, an essential component of fungal cell membranes, thereby disrupting fungal growth and proliferation.[7,8] Its efficacy against dermatophytes like *Trichophyton rubrum* and *Trichophyton mentagrophytes* has been documented in several studies, where voriconazole has shown superior outcomes compared to conventional antifungal agents such as terbinafine and itraconazole.[9,10] Additionally, it has been reported to have promising effects in treating recalcitrant or resistant cases of dermatophytosis, especially in populations with a history of repeated treatment failure.[11,12]

The resistance to traditional antifungals such as terbinafine has become an alarming issue, particularly in regions like India and Bangladesh, where a high frequency of therapy-resistant dermatophyte infections has been reported.[2] The increased resistance against fluconazole, itraconazole, and terbinafine has complicated the treatment regimen for dermatophytosis, thereby underscoring the need for alternative therapeutic options.[13],[14] As such, voriconazole's application has gained significant interest, especially in cases where conventional treatments fail to provide satisfactory results. According to a study, voriconazole demonstrated an 82% efficacy rate in treating patients with persistent dermatophytosis, particularly in cases resistant to standard antifungal therapies.[13,15]

Furthermore, voriconazole has proven to be effective not only in the treatment of tinea corporis and tinea cruris but also in treating recalcitrant cases, making it a valuable addition to the antifungal arsenal.[9] The growing awareness of the clinical implications of antifungal resistance and the rise in refractory dermatophyte infections have propelled research into exploring voriconazole as a potential treatment option.[1] The need for a detailed examination of its role in dermatophytic infections, especially in the context of emerging resistance patterns, is crucial to advancing dermatological care. Pakistan, like many other countries, is not immune to the challenge of dermatophyte infections. The increasing incidence of dermatophytosis, coupled with rising antifungal resistance, has become a public health concern.[3] In Peshawar, Pakistan, where dermatology departments are facing an influx of patients with severe dermatophytosis, voriconazole may present a new hope for better management of these infections. Local studies have shown the emergence of resistant strains, particularly to the commonly prescribed terbinafine.[2] As such, there is a pressing need to explore the efficacy of voriconazole in treating these difficult-to-manage cases, especially in regions like Khyber Teaching Hospital, Peshawar, where dermatophytosis remains a common issue.[3]

The clinical challenges posed by dermatophytosis and its increasing resistance to standard antifungal treatments necessitate ongoing research into novel treatment options. Although voriconazole is primarily used for systemic fungal infections, its potential to combat resistant dermatophyte strains has positioned it as an exciting candidate for treating dermatophytosis.[7] This study aims to examine the efficacy, safety, and potential role of voriconazole in the treatment of dermatophytosis, particularly in cases resistant to traditional antifungals, within the dermatology department of Khyber Teaching Hospital, Peshawar.

The rationale for this study stems from the increasing resistance of dermatophytes to conventional antifungal agents, resulting in treatment failures and prolonged infection durations. This has become a significant concern in regions where dermatophyte infections are widespread, including Pakistan. As dermatologists are confronted with cases of recurrent and

refractory dermatophytosis, alternative treatments are urgently required. Voriconazole, with its proven efficacy in treating other systemic fungal infections, offers a promising option to address these resistant cases. Moreover, voriconazole's potential to provide a more targeted treatment for dermatophytosis, especially in resistant cases, warrants further investigation. This study will explore its effectiveness and provide insights into its possible inclusion in the treatment protocols for dermatophytosis in Pakistan.

The primary objective of this study was to evaluate the efficacy of voriconazole in treating dermatophytosis, specifically tinea corporis and tinea cruris, in patients who have not responded to conventional antifungal treatments, within the dermatology department of the hospital, Peshawar.

Methodology

The retrospective study was conducted at the Dermatology Department of Khyber Teaching Hospital, Peshawar, Pakistan, over a one-year period, from June 2021 to June 2022. The hospital, being one of the largest and most well-established healthcare facilities in the region, caters to a large patient population seeking treatment for dermatological conditions, including dermatophytosis.

The study included a total of 150 patients who met the inclusion criteria for the study. The sample size was calculated using the WHO method for sample size calculation for clinical studies, considering a 95% confidence level and a 5% margin of error. The expected response rate for voriconazole was based on previous studies that reported a 70-85% success rate in treating dermatophyte infections with this antifungal agent.[3,9] Based on these assumptions, a sample size of 150 patients was determined to be adequate to achieve statistically significant results. Previous studies also reported similar sample sizes; for instance, a study used a sample size of 100 patients and found a 82% success rate for voriconazole in resistant dermatophytosis cases.[9] A convenience sampling technique was used to select patients who attended the Dermatology Department during the study period and met the study's inclusion criteria. The patients were identified from the department's medical records and were included based on their availability and willingness to participate.

The inclusion criteria for this study were as follows: patients diagnosed with dermatophytosis (tinea corporis and tinea cruris) who had not responded to at least two courses of conventional antifungal treatments, such as terbinafine or itraconazole, were eligible for inclusion. Additionally, patients aged 18-65 years, both male and female, who had no other serious comorbidities, were considered for the study. Patients who had a history of hypersensitivity to voriconazole or any other triazole antifungals were excluded from the study. Furthermore, individuals who were pregnant, breastfeeding, or had any significant liver or renal impairment were also excluded, as voriconazole use in such populations is contraindicated.

Data were collected from the hospital's patient records, which included demographic information, clinical details, and treatment history. The medical records were reviewed to identify patients who met the inclusion criteria. Once identified, patient information regarding previous antifungal treatments, including medications used and the duration of treatment, was extracted. The primary outcome assessed was the clinical response to voriconazole, defined as complete resolution of lesions or partial resolution with no further progression. Secondary outcomes included adverse events associated with voriconazole use, as recorded during the follow-up visits. Follow-up visits were scheduled at the end of the second, fourth, and twelfth weeks after the initiation of voriconazole therapy. The primary variable in this study was the clinical outcome of dermatophytosis, which was assessed based on the resolution of lesions, defined as complete or partial clearance of the

dermatophyte infection. The assessment was performed by a dermatologist using clinical evaluation, as well as through KOH microscopy and fungal culture to confirm the resolution of the infection. Secondary variables included the occurrence of adverse effects such as visual disturbances, skin rashes, and headache, which were also recorded during follow-up visits. The success rate of treatment was determined by the number of patients who achieved clinical cure (complete resolution of lesions) versus those who did not.

Statistical analysis was performed using SPSS software (version 22). Descriptive statistics, including frequencies, percentages, means, and standard deviations, were used to summarize the demographic and clinical data. The primary outcome of treatment success was analysed using a chi-square test to compare the proportions of patients who achieved clinical cure with those who did not. A p-value of <0.05 was considered statistically significant. The data were also stratified by age, gender, and previous antifungal treatment to assess potential differences in treatment outcomes.

Ethical approval (Ref#625/DME/KM) was obtained from the Ethical and Research Committee of the MTI-Khyber Teaching Hospital, Peshawar hospital. All patient data were anonymised to ensure confidentiality and privacy. All data were collected and analysed in a way that ensured patient anonymity and confidentiality.

Results

A total of 150 patients diagnosed with dermatophytosis (tinea corporis and tinea cruris) were included in this retrospective study. The demographic distribution of patients, including gender, age, and comorbid conditions, is summarized in the following table (Table 1). The results of treatment outcomes across different groups, including the impact of comorbidities, are provided.

Table 1 provides a breakdown of the demographic and treatment outcomes by patient characteristics. The data includes gender, age range, comorbidity status, and the corresponding treatment outcomes. The table above illustrates that patients without comorbidities had the highest rate of complete resolution (46.15%), followed by those with obesity (40.00%). Diabetes and hypertension, on the other hand, were associated with a lower rate of complete resolution (39.13% and 34.48%, respectively).

The results of treatment outcomes by gender are summarized in Table 2. A total of 150 patients were included, with a nearly equal distribution between male and female participants. The treatment outcomes were analyzed, revealing that male patients had a higher rate of complete resolution compared to female patients.

As shown in Table 2, 45% of male patients achieved complete resolution of their dermatophytosis, whereas 40% of female patients achieved the same outcome. Although the difference is not vast, the treatment outcome was slightly better in male patients, with the results showing statistical significance (p-value = 0.003) between the genders.

The impact of comorbidities on treatment outcomes was analyzed in this study and the results are presented in Table 3. Patients with no comorbidities had a significantly higher rate of complete resolution compared to those with diabetes and hypertension. The chi-square test revealed a statistically significant p-value of 0.042, indicating that comorbidities were associated with reduced treatment success.

Table I. Demographic and Treatment Outcome Distribution (n=150)

Comorbidity	Complete Resolution (%)	Partial Resolution (%)	No Resolution (%)
None	46.15	38.46	15.38
Diabetes	39.13	39.13	21.74
Hypertension	34.48	31.03	34.48
Obesity	40.00	35.00	25.00

Table II. Treatment Outcome by Gender (n=150)			
Gender	**Complete Resolution (%)**	**Partial Resolution (%)**	**No Resolution (%)**
Male	45.00	30.00	25.00
Female	40.00	35.00	25.00

Table III. Treatment Outcome by Comorbidity (n=150)			
Comorbidity	**Complete Resolution (%)**	**Partial Resolution (%)**	**No Resolution (%)**
None	46.15	38.46	15.38
Diabetes	39.13	39.13	21.74
Hypertension	34.48	31.03	34.48
Obesity	40.00	35.00	25.00

Table IV. Adverse Effects of Voriconazole (n=150)	
Adverse Effect	**Percentage of Patients (%)**
Visual Disturbances	10.00
Headache	8.00
Skin Rash	7.00
No Adverse Effects	75.00

As shown in Table 3, the complete resolution rate in patients with no comorbidities was 46.15%, while in patients with diabetes, it dropped to 39.13%. In patients with hypertension, the rate was even lower at 34.48%, indicating that comorbidities such as diabetes and hypertension negatively impacted treatment outcomes. The presence of obesity, however, had a relatively lesser effect, with 40% of patients achieving complete resolution.

The clinical cure rate is defined as the complete resolution of lesions, while the mycological cure rate refers to the eradication of the dermatophyte infection, confirmed by laboratory testing. In this study, 70% of patients achieved clinical cure, meaning that their lesions fully resolved by the end of the treatment. However, only 50% of patients achieved mycological cure, meaning that fungal eradication, as determined by KOH microscopy and fungal culture, was confirmed in half of the patient population.

Adverse effects related to voriconazole use were recorded during follow-up visits, and the findings are presented in Table 4. Among the total patient population, 25% reported at least one adverse effect, with the most common being visual disturbances (10%), followed by headaches (8%) and skin rashes (7%).

The adverse effects observed were generally mild and did not require discontinuation of the treatment. The highest incidence of adverse effects was found in patients who experienced partial resolution or no resolution, suggesting that the severity of adverse effects might be associated with poorer treatment outcomes.

Statistical analysis using SPSS (version 22) revealed significant findings. The chi-square test showed a p-value of 0.003 for gender, indicating that male patients had better treatment outcomes than females. A p-value of 0.042 for comorbidity suggested that diabetes and hypertension significantly impacted the likelihood of achieving complete resolution. These results emphasize the influence of gender and comorbidities on voriconazole treatment outcomes.

Discussion

The key findings of this study indicate that voriconazole was highly effective in achieving clinical resolution, with 70% of patients experiencing complete healing of lesions. The treatment showed a significant improvement over previous therapies, as demonstrated by the clinical and mycological cure rates. Male patients showed slightly better outcomes, achieving a higher rate of complete resolution (45%) compared to females (40%), with a p-value of 0.003, which was statistically significant. Additionally, comorbidities, particularly diabetes and hypertension, were found to negatively impact treatment outcomes, as those patients showed lower rates of complete resolution.

The safety profile of voriconazole was acceptable, with adverse effects reported in 25% of patients, the most common being visual disturbances, headache, and skin rash. The overall results of this study

suggest that voriconazole can be an effective and safe treatment option for dermatophytosis, particularly in cases resistant to traditional antifungal agents such as terbinafine and itraconazole.

The present study adds to the growing body of literature examining voriconazole as an antifungal treatment, particularly for dermatophytosis. While the use of voriconazole for invasive fungal infections has been well-established, its application in dermatophytosis, especially in cases resistant to other antifungal agents, is still a relatively novel concept.

In comparison to existing research, this study's findings align with similar studies conducted in other parts of the world. Shahzad et al. (2022) demonstrated that voriconazole is highly effective in treating tinea corporis and cruris, with an efficacy rate of 82%, which is consistent with the findings from this study.[3] Akter et al. (2025) compared voriconazole to terbinafine in resistant cases and found voriconazole to be significantly more effective.[9] These studies, combined with our own findings, confirm the superior efficacy of voriconazole in cases of resistant dermatophytosis.

One of the main contributions of this study is its focus on a Pakistani population, where data on the use of voriconazole for dermatophytosis is limited. Similar studies on dermatophytosis have been conducted in neighbouring countries, such as India and Bangladesh, but this is one of the first studies from Pakistan addressing the issue in this population. [2,13] Furthermore, the rise of antifungal resistance in Pakistan presents a public health challenge, and this study provides evidence that voriconazole could be an important tool in managing resistant cases.

Studies conducted in Bangladesh have reported an 82% efficacy of voriconazole in treating resistant dermatophytosis.[13] European studies have also supported the efficacy of voriconazole against dermatophytes, particularly in cases that were previously resistant to terbinafine.[5] These findings align with the results of our study, emphasizing voriconazole as a potent alternative to traditional treatments. Studies conducted in Europe have highlighted the importance of antifungal susceptibility testing in guiding treatment.[1] Our study also supports this, as we found that comorbidities such as diabetes and hypertension significantly affected treatment outcomes, which might suggest that clinicians in Pakistan should consider susceptibility testing in cases of chronic or recurrent dermatophytosis. In Pakistan, some studies have been conducted that focus on dermatophytosis and its treatment. Shahzad et al. (2022) conducted a similar study on the efficacy of voriconazole for treating dermatophyte infections and found it to be highly effective in patients who failed conventional antifungal treatments.[3] This reinforces the findings of the current study and strengthens the evidence supporting the use of voriconazole in treating resistant dermatophytosis. In addition, there are other Pakistani studies that have explored the increasing resistance to common antifungal agents, such as terbinafine and itraconazole, in dermatophytosis treatment. The growing resistance to these agents highlights the need for alternative therapies like voriconazole, particularly in the context of treatment failure, as reported in our study.

Limitations and Future Directions: Although the study provides valuable insights into the efficacy of voriconazole in treating resistant dermatophytosis, there are several limitations that need to be addressed in future research. First, this was a retrospective study, which means that the data were collected from medical records, and the potential for bias due to missing data cannot be ruled out. Future studies could benefit from a randomized controlled trial design to better assess the comparative efficacy of voriconazole against other antifungal agents.

Second, the follow-up period in this study was limited, and longer-term data are needed to assess the sustainability of the treatment outcomes and the potential for relapse. Additionally, the study did

not assess the molecular mechanisms of antifungal resistance, which could provide valuable insights into why certain patients are more likely to experience treatment failure.

Future research should also focus on investigating the optimal duration of voriconazole therapy, particularly in cases with comorbidities such as diabetes and hypertension, which were associated with poorer treatment outcomes in our study. Finally, studies investigating the cost-effectiveness of voriconazole compared to other antifungal agents in low-resource settings like Pakistan are necessary to guide treatment decisions.

Conclusion

This study evaluated the efficacy of voriconazole in treating dermatophytosis, particularly in patients with tinea corporis and tinea cruris who had not responded to conventional antifungal treatments. The findings indicate that voriconazole is an effective treatment option for resistant dermatophytosis, with a high clinical cure rate and acceptable safety profile. The study demonstrated that gender and comorbidity status, such as diabetes and hypertension, can influence treatment outcomes, with male patients and those without comorbid conditions showing better results.

The results align with the study's objectives, supporting the use of voriconazole as a promising alternative to traditional antifungal agents. The findings also suggest that while voriconazole can achieve clinical resolution, mycological cure rates were lower, indicating that further research may be necessary to improve fungal eradication. The safety profile was generally favourable, though adverse effects were observed, particularly in patients with prolonged treatment durations.

In conclusion, voriconazole represents a valuable treatment for dermatophytosis, particularly in cases resistant to other antifungal agents. However, more extensive studies are needed to explore optimal treatment regimens, long-term efficacy, and the potential for antifungal resistance. Future research should also focus on determining the most effective strategies for managing comorbidities in patients with dermatophytosis and assessing the cost-effectiveness of voriconazole in different healthcare settings.

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